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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,708	02/20/2001	Akiko Itai	P20294	4541

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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/700,708

Applicant(s)

ITAI ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 5-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5/9/2003. 6) ☐ Other: _____

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DETAILED ACTION

Status of Claims

1. Amendment filed 09/05/2003 is acknowledged. Claims 1-4 are canceled. Claims 5-8 are pending and are amended.

Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn. The following rejections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons:

New rejections

- A. Claim 5 is ambiguous in that it requires, first, to determine homology based on coincidence of each residue; and then requires determination alignment based on

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homology of only selected sites of the protein molecule. It is not clear whether all or selected residues are needed.

B. At claim 5, lines 7-8, the term "importance score is high" is indefinite because it is a relative term, but no standard of reference has been provided with which to determine whether a particular score is "high" or not. Accordingly, it is not possible to determine what sites are embraced within the scope of the claimed method of preparing alignment. Same in claim 6, line 4

C. Claim 5, last paragraph: It is not clear how an Importance score reflects relation of a given residue to many biological functions of the protein.

D. The term "template protein" in claim 7 lacks antecedent basis as the base claim does not recite "template protein". Further, it is not clear how many of "each" template proteins are meant.

Maintained rejections

E. Claim 6: The previous Office action stated that the claim addresses method further comprising "searching correspondences" for groups of two or more continuous amino acid residues. Does it mean that searching for groups of two or more continuous amino acid residues is done in addition to calculating of homology based on coincidence of each amino acid under consideration, as claimed in the base claim 5?

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Applicant directs examiner's attention to p. 11. However, while claim 5 requires calculation of homology for entire protein, p. 11 discusses determining homology for specific sites. (On a different matter: it seems that incorporating language of p. 11, lines 11-15 (from... homology to ...best) into claims might make them clearer).

F. Claim 7: The claim recites "final score of homology". It is not clear how such score is different from homology score already calculated according to the base claim 5: No new steps which would alter the homology score are addressed in the claim.

Applicant directs examiner's attention to pages 11,12. However, the paragraph bridging the pages merely reiterates the language of the claim; the meaning of the latter remains unclear. Furthermore the term "scale factor" is not defined in the disclosure and it is not clear how (and why) the resulting data are being modified.

Claim Rejections - 35 USC § 112, first paragraph.

3. Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparing alignment for limited segments of protein sequences, does not reasonably provide enablement for preparing alignment for full-length protein sequences.

The claims as amended require use of a known database protein wherein for every single residue of the known protein there is an information on the importance

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of this given residue in relation to one or more biological functions known for this protein.

The only working examples, examples 1 and 2, pages 14-16, are drawn to use of database containing information for several enzymes. For each of the enzymes, an importance score was generated for each amino acid residue based on the distance from a putative inhibitor or coenzyme. Note that, as no data reflecting the said importance score for said each residue are present in the disclosure, it is not clear what these data are actually reflect because each of the named enzymes has a plurality of inhibitors and co-enzymes, each of which will have different set of interacting residues. At best, the generated data will represent "importance score" for a particular domain while leaving the majority of the protein sequence unannotated. The specification does provide general guidance on determining "importance score" using criteria other than distance from a particular residue (pages 9,10); however, again, other methods would yield information on importance of residues of a particular domain or epitope, but not on every and each residue of a complex multi-functional protein molecule. While it is well known in the art how to improve accuracy of protein alignment by accounting for essence of amino acid residues of a particular domain (see, e.g., Guigo et al; submitted by applicants), the art is unpredictable about use of sequences wherein each and every residue contain associated information on its "importance" for particular function. This is because,

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first, proteins are large multi-functional molecules having different domains involved in different functions, and, second, because, as stated in Guigo, "protein databases are characterized by a relatively high degree of noise and uncertainty", which would not allow determining importance for each residue.

Furthermore, the claims are drawn to using "importance scores" regarding more than one biological function. The specification is devoid of examples or guidance on preparing alignment using importance score reflecting various (more than one) functions, as well as examples or guidance on how to determine importance score reflecting involvement of a given residue in a plurality of biological functions.

Further, while it seems plausible to determine geometrical distance for each residue to a putative ligand or inhibitor, such geometrical distance is not directly related to an importance for the appearance of a biological function. As to the relevance of each residue for the appearance of a real biological function (rather than distance in a crystal), such determination for each residue of a complex molecule would require a lengthy and undue experimentation.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

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Claim Rejections - 35 USC § 102.

4. Rejection of claims 5-8 under 35 U.S.C. 102(b) over Chen et al. is withdrawn in view of insufficient date of the reference demonstrated by applicant.

Prior art made of record

5. The references of Guigo et al. is considered pertinent to applicant's invention and was provided by applicants. The reference teaches method of determining correlation between database protein and test protein by combining sequence alignment with use of appropriate attributes for residues of the database protein, and finding the closest subset of the database to the test protein. The difference of the referenced method is that it does not require information on biological function for each amino acid residue of the database sequence.

Conclusion.

6. No claims are allowed

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

December 5, 2003

mlb

